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Current Status of Research Progress on Idiopathic Pulmonary Fibrosis

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Abstract: Idiopathic pulmonary fibrosis (IPF) is a chronic, irreversible interstitial lung disease characterized by diffuse pulmonary interstitial fibrosis and progressive decline in pulmonary function, with its etiology not yet fully elucidated. The pathological process primarily manifests as recurrent injury and abnormal repair of alveolar epithelial cells, sustained activation of fibroblasts, leading to excessive extracellular matrix deposition and structural remodeling of lung tissue in patients. This review focuses on the pathological features, pathogenesis, and key signaling pathways of IPF, systematically summarizing current major clinical treatment strategies to provide theoretical references for further elucidation of IPF pathogenesis and exploration of more effective prevention and therapeutic approaches.

Keywords: Idiopathic pulmonary fibrosis; Pulmonary fibroblasts; Pathogenesis; Signaling pathways; Anti-fibrotic therapy

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1. Introduction

IPF is the most common and worst-prognosed subtype of idiopathic interstitial pneumonia, characterized by complex pathogenesis involving multiple cellular and molecular processes. The median survival after diagnosis is 3–5 years, with a rising global mortality rate [1]. The core pathological feature of IPF involves repair dysregulation following persistent alveolar epithelial cell injury, leading to abnormal proliferation of pulmonary fibroblasts and extensive differentiation into pulmonary myofibroblasts. This results in extracellular matrix (ECM) deposition in the pulmonary interstitium, ultimately forming a “honeycomb lung” structure and impairing gas exchange function [2].

Due to the insidious early symptoms of IPF, clinical diagnosis is often confused with chronic obstructive pulmonary disease (COPD) and heart failure, with approximately 60% of patients diagnosed at intermediate or advanced stages [3]. Currently, there is no curative treatment for IPF. Pirfenidone and nintedanib, as commonly used anti-fibrotic agents, can slow pulmonary function decline but are associated with significant tolerance issues [4]. Existing therapies can only delay disease progression, underscoring the clinical importance of investigating IPF’s pathological mechanisms and therapeutic targets. This article summarizes the pathological characteristics, pathogenesis, key signaling pathways, and current treatment options for IPF to provide theoretical foundations for exploring effective therapeutic strategies.

2. Pathological Characteristics of IPF

2.1. Pulmonary interstitial fibrosis

Pulmonary interstitial fibrosis is the most typical pathological feature of IPF, and its progression can be divided into three stages: "damage-inflammation-repair imbalance." After alveolar epithelial cells are injured by external stimuli, their barrier function is compromised, leading to the release of pro-inflammatory factors and pro-fibrotic factors. Inflammatory cells are recruited to the injury site, exacerbating local inflammatory responses. Pulmonary fibroblasts are activated and differentiate into myofibroblasts, which synthesize large amounts of collagen, fibronectin, and other extracellular matrix (ECM) components. Additionally, the activity of ECM degradation enzymes is inhibited, resulting in excessive ECM deposition in the pulmonary interstitium [5–7].

2.2. Inflammatory cell infiltration

The immune-inflammatory response serves as a critical defense mechanism of the body and an essential phase in injury repair, maintaining normal physiological functions of tissues and organs by resisting various injuries and infections. Abnormal injury repair is a primary pathological feature of idiopathic pulmonary fibrosis (IPF). The immune-inflammatory response plays a pivotal driving role in the early stages of IPF pathogenesis, where activated inflammatory cells secrete various inflammatory mediators to trigger inflammatory responses, thereby inducing dysregulation of injury healing during IPF progression [8]. Studies have revealed a significant increase in macrophage count in alveolar lavage fluid from IPF patients [9]. Macrophages participate in inflammatory regulation, pulmonary tissue injury, and repair through two core pathways, classical polarization and alternative activation—thereby influencing the onset and progression of IPF [10,11].

3. Pathogenesis of IPF

3.1. Alveolar epithelial cell injury and epithelial-mesenchymal transition

Alveolar epithelial cell injury represents the initial pathological step in the pathogenesis of idiopathic pulmonary fibrosis (IPF), with dysfunction of type II alveolar epithelial cells (AEC II) serving as the core etiological factor. In IPF, oxidative stress, telomere shortening, and genetic mutations may induce "senescence phenotypes" in AEC II, characterized by reduced proliferative capacity, secretory dysfunction, and increased apoptosis [12,13]. Damaged AEC II can undergo "epithelial-mesenchymal transition" to transform into myofibroblasts. Under the influence of factors such as TGF-β1 and IL-1β, AEC II lose epithelial markers and acquire migratory capabilities, subsequently secreting extracellular matrix (ECM) upon entering the pulmonary interstitium, thereby promoting the progression of IPF [14,15].

3.2. Activation and proliferation of lung fibroblasts

The activation of pulmonary fibroblasts is a pivotal step in the fibrotic process of IPF, and its activation is regulated by multiple factors. Resting pulmonary fibroblasts exhibit weak ECM synthesis capacity; upon stimulation by pro-fibrotic factors such as TGF-β1 and PDGF, they can activate intracellular signaling pathways, differentiate into myofibroblasts, and secrete large amounts of ECM, thereby exacerbating pulmonary fibrosis accumulation [16]. TGF-β1, as a key cytokine responsible for fibrosis [17], binds to TGF-β receptors on the membrane of pulmonary fibroblasts, activating both Smad-dependent and non-Smad pathways, which promote the expression of downstream fibrotic target genes and drive the progression of pulmonary fibrosis [18,19].

2.3. ECM remodeling imbalance

Abnormally activated fibroblasts extensively synthesize extracellular matrix components such as collagen and fibronectin, leading to ECM structural remodeling. In IPF patients, the dynamic balance between matrix metalloproteinases and tissue inhibitor of metalloproteinases is disrupted, thereby impairing the normal degradation capacity of ECM and promoting its

persistent abnormal deposition in lung tissue, ultimately accelerating the onset and progression of pulmonary fibrosis [20].

2.4. Oxidative stress and cellular damage

Oxidative stress is a significant predisposing factor for the pathogenesis of IPF, with its core mechanism involving an imbalance between reactive oxygen species (ROS) generation and clearance in lung tissue. Excessive ROS directly induces oxidative damage to DNA, proteins, and lipids, ultimately leading to cellular injury. In IPF patients, oxidative stress responses in lung tissues are markedly enhanced, characterized by excessive accumulation of superoxide anions and hydrogen peroxide, coupled with dysregulation of the body's antioxidant defense systems, which accelerates pulmonary fibrosis progression [21]. Additionally, multiple oxidative stress-related signaling pathways exhibit aberrant regulation in IPF. Activation of the NF-κB pathway promotes the release of various pro-inflammatory factors, while Nrf2 activity is significantly reduced in IPF patients, resulting in impaired clearance of excess ROS. This creates a vicious cycle of oxidative damage and repair dysregulation, driving sustained progression of pulmonary fibrosis [22].

2.5. Immune inflammatory response

In patients with idiopathic pulmonary fibrosis (IPF), the number of various inflammatory cells, such as macrophages, T lymphocytes, and neutrophils in lung tissue is significantly increased [23], releasing large amounts of TNF-α and IL-6 to trigger inflammatory responses [24], exacerbating pulmonary tissue damage. B lymphocytes and T lymphocytes in the lung tissue of IPF patients exhibit extensive abnormal activation, leading to the production of autoantibodies and immune complex formation, which further aggravate inflammatory reactions and pulmonary tissue injury [25,26]. During the early stage of alveolar epithelial cell (AEC) injury, neutrophils are extensively recruited to the injury site, where they release pro-inflammatory mediators and neutrophil elastase (NE) to stimulate downstream immune responses, thereby inducing abnormal repair of damaged tissues during IPF progression. Additionally, NE accelerates the formation of pulmonary scar tissue and the progression of pulmonary fibrosis by promoting fibroblast proliferation and differentiation, inducing myofibroblast activation, and upregulating α-SMA expression [27,28].

3. IPF-related signaling pathways

3.1. TGF-β/Smad signaling pathway

The TGF-β/Smad signaling pathway is a critical pathway in the pathogenesis of fibrosis. TGF-β1, as a key stimulatory factor [29], plays a significant role in pulmonary fibrosis. By activating the Smad signaling pathway, TGF-β1 promotes the proliferation, activation, and migration of pulmonary fibroblasts, as well as upregulates collagen synthesis and secretion, thereby advancing the progression of idiopathic pulmonary fibrosis (IPF) [30]. The Smad-dependent signaling pathway is a classical mechanism underlying the development of IPF. In IPF patients, the TGF-β/Smad signaling pathway is abnormally activated in lung tissues, with significantly elevated levels of TGF-β1. TGF-β1 binds to TGF-βRII, inducing its phosphorylation and recruiting TGF-βRI, which subsequently activates downstream Smad2/3 proteins. These proteins then form complexes with Smad4, translocating from the cytoplasm to the nucleus, where they bind to promoter regions of target genes such as COL1A1, α-SMA, and Snail, regulating gene expression and promoting extracellular matrix (ECM) synthesis and epithelial-mesenchymal transition (EMT) processes [31,32].

3.2. Wnt/β-catenin signaling pathway

The Wnt/β-catenin signaling pathway plays a critical role in embryonic development and tissue repair, with its abnormal activation being closely associated with the fibrotic process in idiopathic pulmonary fibrosis (IPF). Under normal conditions, cytoplasmic β-catenin is phosphorylated and degraded by a complex composed of glycogen synthase kinase-3β (GSK-3β) and AXIN, keeping the pathway in an inhibited state. During IPF development, this pathway becomes activated. In IPF patients, expression levels of Wnt3a, β-catenin, and their target genes are significantly elevated in lung tissues. Wnt

ligands such as Wnt3a and Wnt5a bind to cell membrane receptors Frizzled/LRP5/6, inhibiting GSK-3β protein activity. Consequently, β-catenin fails to be effectively degraded, leading to persistent accumulation in the cytoplasm. Upon entering the nucleus in large quantities, it binds to downstream transcription factors, thereby regulating the proliferation and differentiation of pulmonary myofibroblasts and influencing the fibrotic process [33].

3.3. Hippo/YAP/TAZ signaling pathway

The Hippo/YAP/TAZ signaling pathway is a critical pathway regulating cell proliferation, apoptosis, and organ size. Recent studies have revealed its significant role in idiopathic pulmonary fibrosis (IPF). In IPF, excessive deposition of pulmonary interstitial extracellular matrix (ECM) inhibits Hippo pathway activity, leading to sustained activation of YAP/TAZ. Activated YAP/TAZ promotes pulmonary fibroblast proliferation and ECM synthesis, induces alveolar epithelial cell senescence, and suppresses reparative functions. Research has demonstrated that YAP gene knockout significantly alleviates pulmonary fibrosis in mice, suggesting that YAP/TAZ may represent a potential therapeutic target for IPF [34].

3.4. JAK/STAT signaling pathway

In IPF, the JAK/STAT signaling pathway is abnormally activated, regulating the upregulation of downstream pulmonary fibrosis-related genes, leading to increased synthesis of collagen and fibronectin, and reducing ECM degradation by inhibiting MMP expression or promoting TIMP expression. This results in excessive ECM deposition in IPF, exacerbating disease progression [35]. The JAK/STAT signaling pathway synergistically promotes fibroblast proliferation and activation while inhibiting the AECs' repair, thereby advancing pulmonary fibrosis [36]. Studies have demonstrated that IL-6 and IL-10 activate JAK2 and STAT3, promoting fibroblast proliferation and differentiation into myofibroblasts, increased ECM synthesis, and subsequent excessive deposition, thereby aggravating the pathological course of IPF [37]. Furthermore, research confirms that IL-27 significantly downregulates JAK/STAT signaling pathway activation by inhibiting STAT1 and STAT5 phosphorylation, thereby delaying IPF progression [38]. These findings indicate that JAK/STAT signaling pathway-targeted therapeutic strategies hold significant clinical potential in the treatment of pulmonary fibrosis.

3.5. PI3K/AKT signaling pathway

In patients with idiopathic pulmonary fibrosis (IPF), the expression of PI3K and AKT in lung tissue is significantly elevated. The key pathogenic factor TGF-β in IPF activates the PI3K/AKT signaling pathway, inhibiting apoptosis of alveolar epithelial cells (AECs) and enhancing their migratory capacity. Excessive migration and survival lead to abnormal phenotypic transformation of AECs, thereby promoting the occurrence and progression of epithelial-mesenchymal transition (EMT) and exacerbating IPF development. Tetrahydroindene (TET), as an intervention agent for the PI3K/AKT signaling pathway, can significantly ameliorate silica-induced pulmonary fibrosis models. Studies have demonstrated that TET can target and regulate the PI3K/AKT signaling pathway, downregulating the expression levels of fibrosis-related biomarkers, providing novel therapeutic targets and strategic directions for pulmonary fibrosis treatment [39].

3.6. MAPK signaling pathway

Extracellular signal-regulated kinase ERK, p38 mitogen-activated protein kinase, and c-Jun N-terminal kinase are components of the MAPK pathway. The ERK signaling pathway promotes fibroblast proliferation and activation, increases extracellular matrix (ECM) synthesis, and drives the progression of idiopathic pulmonary fibrosis (IPF). In bleomycin-induced IPF rat models [40], the expression levels of ERK1 and ERK2, key members of the ERK signaling pathway, were significantly upregulated, confirming their critical regulatory roles in the pathological process of pulmonary fibrosis. In bleomycin-induced IPF models [41], JNK expression levels were markedly elevated. The JNK signaling pathway contributes to IPF development by promoting abnormal fibroblast activation, facilitating myofibroblast differentiation, increasing ECM synthesis and secretion, and regulating the release of pro-inflammatory cytokines such as TNF-α and IL-6.

4. Current treatment options for IPF

4.1. Anti-fibrotic drug therapy

Currently, there are no effective drugs available for the treatment of IPF. Pirfenidone and nintedanib are the primary medications capable of alleviating IPF symptoms [42]. These agents exert their therapeutic effects by inhibiting pulmonary fibroblast activation and ECM synthesis, thereby delaying IPF progression, reducing the risk of acute exacerbations, and lowering mortality rates [43].

Pirfenidone inhibits the TGF-β/Smad signaling pathway, reduces the secretion of fibrogenic factors and pro-inflammatory factors, thereby suppressing abnormal proliferation and activation of pulmonary fibroblasts, decreasing fibroblast differentiation into myofibroblasts, reducing collagen synthesis, and prolonging patient survival [44]. Nintedanib blocks downstream signal transduction processes by targeting PDGF receptors, FGFR receptors, and VEGF receptors. Nintedanib inhibits PDGF-mediated fibroblast proliferation and migration, suppresses FGFR-mediated ECM synthesis, inhibits VEGF-mediated angiogenesis, and alleviates pulmonary interstitial inflammation [45].

4.2. Pulmonary rehabilitation and supportive therapy

Pulmonary rehabilitation therapy is currently an effective method for alleviating IPF, capable of improving patients' dyspnea symptoms, enhancing exercise tolerance, and improving quality of life. IPF patients can improve their quality of life through respiratory training, exercise training, psychological intervention, and oxygen therapy. Supportive treatments also include preventing pulmonary infections, such as influenza vaccination and pneumococcal vaccination, managing comorbidities like gastroesophageal reflux disease, and utilizing proton pump inhibitors for treatment. These measures can reduce the risk of acute exacerbations in IPF and improve patient prognosis [46].

5. Conclusion

IPF is a disease characterized by complex pathogenesis, poor prognosis, and relatively limited treatment options. Therefore, an in-depth understanding of its pathogenesis and pathological features holds significant theoretical importance for the development of novel therapeutic agents. This article focuses on multiple signaling pathways closely associated with IPF, including TGF-β/Smad and Wnt/β-catenin pathways. These pathways collectively influence key pathological processes, such as fibroblast activation, extracellular matrix metabolism imbalance, and inflammatory responses, thereby promoting the onset and progression of pulmonary fibrosis. However, the pathogenesis of IPF remains complex. Future research requires systematic exploration of the regulatory mechanisms of these signaling pathways to provide critical theoretical foundations for screening novel biomarkers for early disease diagnosis and identifying clinically valuable therapeutic targets. This will further advance the development of precision diagnosis and treatment systems for IPF and improve the quality of life for the patients.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Podolanczuk AJ, Thomson CC, Remy-Jardin M, et al., 2023, Idiopathic Pulmonary Fibrosis: State of the Art for 2023. Eur Respir J, 61(4): 2200957.

[2] Mei Q, Liu Z, Zuo H, et al., 2022, Idiopathic Pulmonary Fibrosis: An Update on Pathogenesis. Front Pharmacol, 12: 797292.

[3] Ley B, Collard HR, King TE Jr., 2011, Clinical Course and Prediction of Survival in Idiopathic Pulmonary Fibrosis. Am J

Respir Crit Care Med, 183(4): 431–440.
[4] Maher TM, 2024, Interstitial Lung Disease: A Review. JAMA, 331(19): 1655–1665.
[5] Wynn TA, 2008, Cellular and Molecular Mechanisms of Fibrosis. J Pathol, 214(2): 199–210.
[6] Yu QY, Tang XX, 2022, Irreversibility of Pulmonary Fibrosis. Aging Dis, 13(1): 73–86.
[7] Katzenstein AL, Myers JL, 1998, Idiopathic Pulmonary Fibrosis: Clinical Relevance of Pathological Classification. Am J Respir Crit Care Med, 157(4 Pt 1): 1301–1315.
[8] Fathimath M, Shaikh SB, Jeena TM, et al., 2021, Inflammatory Mediators in Various Molecular Pathways Involved in the Development of Pulmonary Fibrosis. Int Immunopharmacol, 96: 107608.
[9] Yin YQ, Peng F, Situ HJ, et al., 2022, Construction of Prediction Model of Inflammation Related Genes in Idiopathic Pulmonary Fibrosis and Its Correlation With Immune Microenvironment. Front Immunol, 13: 1010345.
[10] Ge Z, Chen Y, Ma L, et al., 2024, Macrophage Polarization and Its Impact on Idiopathic Pulmonary Fibrosis. Front Immunol, 15: 1444964.
[11] Raghu G, Collard HR, Egan JJ, et al., 2011, An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-Based Guidelines for Diagnosis and Management. Am J Respir Crit Care Med, 183: 788–824.
[12] Zhu W, Tan C, Zhang J, 2022, Alveolar Epithelial Type 2 Cell Dysfunction in Idiopathic Pulmonary Fibrosis. Lung, 200(5): 539–547.
[13] Armanios MY, Chen JJ, Cogan JD, et al., 2007, Telomerase Mutations in Families With Idiopathic Pulmonary Fibrosis. N Engl J Med, 356(13): 1317–1326.
[14] Hatipoglu OF, Uctepe E, Opoku G, et al., 2021, Osteopontin Silencing Attenuates Bleomycin-Induced Murine Pulmonary Fibrosis by Regulating Epithelial-Mesenchymal Transition. Biomed Pharmacother, 139: 111633.
[15] Hewlett JC, Kropski JA, Blackwell TS, 2018, Idiopathic Pulmonary Fibrosis: Epithelial-Mesenchymal Interactions and Emerging Therapeutic Targets. Matrix Biol, 71–72: 112–127.
[16] Huang G, Yang X, Yu Q, et al., 2024, Overexpression of STX11 Alleviates Pulmonary Fibrosis by Inhibiting Fibroblast Activation via the PI3K/AKT/mTOR Pathway. Signal Transduct Target Ther, 9(1): 306.
[17] Ma J, Sanchez-Duffhues G, Goumans MJ, et al., 2020, TGF-β-Induced Endothelial to Mesenchymal Transition in Disease and Tissue Engineering. Front Cell Dev Biol, 8: 260.
[18] Sosulski ML, Gongora R, Danchuk S, et al., 2015, Deregulation of Selective Autophagy During Aging and Pulmonary Fibrosis: The Role of TGFβ1. Aging Cell, 14(5): 774–783.
[19] Wang XC, Song K, Tu B, et al., 2023, New Aspects of the Epigenetic Regulation of EMT Related to Pulmonary Fibrosis. Eur J Pharmacol, 956: 175959.
[20] Yu H, Liu S, Wang S, et al., 2024, The Involvement of HDAC3 in the Pathogenesis of Lung Injury and Pulmonary Fibrosis. Front Immunol, 15: 1392145.
[21] Sun Z, Ji Z, Meng H, et al., 2024, Lactate Facilitated Mitochondrial Fission-Derived ROS to Promote Pulmonary Fibrosis via ERK/DRP-1 Signaling. J Transl Med, 22(1): 479.
[22] Dodson M, de la Vega MR, Cholanians AB, et al., 2019, Modulating NRF2 in Disease: Timing Is Everything. Annu Rev Pharmacol Toxicol, 59: 555–575.
[23] Cocconcelli E, Balestro E, Turato G, et al., 2024, Tertiary Lymphoid Structures and B-Cell Infiltration Are IPF Features with Functional Consequences. Front Immunol, 15: 1437767.
[24] Gregory AD, Kliment CR, Metz HE, et al., 2015, Neutrophil Elastase Promotes Myofibroblast Differentiation in Lung Fibrosis. J Leukoc Biol, 98(2): 143–152.
[25] Ren L, Chang YF, Jiang SH, et al., 2024, DNA Methylation Modification in Idiopathic Pulmonary Fibrosis. Front Cell Dev Biol, 12: 1416325.
[26] Kim S, Qin Y, Park HJ, et al., 2024, MOSES: A Methylation-Based Gene Association Approach for Unveiling Environmentally Regulated Genes Linked to a Trait or Disease. Clin Epigenetics, 16(1): 161.
[27] Surendran A, Huang C, Liu L, et al., 2024, Circular RNAs and Their Roles in Idiopathic Pulmonary Fibrosis. Respir Res,

25(1): 77.

[28] Armanios MY, Chen JL, Cogan JD, et al., 2007, Telomerase Mutations in Families with Idiopathic Pulmonary Fibrosis. N Engl J Med, 356(13): 1317–1326.

[29] Derynck R, Budi EH, 2019, Specificity, Versatility, and Control of TGF-β Family Signaling. Sci Signal, 12(570): eaav5183.

[30] Derynck R, Zhang YE, 2003, Smad-Dependent and Smad-Independent Pathways in TGF-Beta Family Signalling. Nature, 425(6958): 577–584.

[31] Hu HH, Chen DQ, Wang YN, et al., 2018, New Insights into TGF-β/Smad Signaling in Tissue Fibrosis. Chem Biol Interact, 292: 76–83.

[32] Peng D, Fu M, Wang M, et al., 2022, Targeting TGF-β Signal Transduction for Fibrosis and Cancer Therapy. Mol Cancer, 21(1): 104.

[33] Shaikh TB, Kuncha M, Andugulapati SB, et al., 2023, Dehydrozingerone Alleviates Pulmonary Fibrosis via Inhibition of Inflammation and Epithelial-Mesenchymal Transition by Regulating the Wnt/β-Catenin Pathway. Eur J Pharmacol, 953: 175820.

[34] Du W, Tang Z, Yang F, et al., 2021, Icariin Attenuates Bleomycin-Induced Pulmonary Fibrosis by Targeting Hippo/YAP Pathway. Biomed Pharmacother, 143: 112152.

[35] Liu J, Wang F, Luo F, 2023, The Role of JAK/STAT Pathway in Fibrotic Diseases: Molecular and Cellular Mechanisms. Biomolecules, 13(1): 119.

[36] Gu S, Liang J, Zhang J, et al., 2023, Baricitinib Attenuates Bleomycin-Induced Pulmonary Fibrosis in Mice by Inhibiting TGF-β1 Signaling Pathway. Molecules, 28(5): 2195.

[37] Onorati A, Havas AP, Lin B, et al., 2022, Upregulation of PD-L1 in Senescence and Aging. Mol Cell Biol, 42(10): e0017122.

[38] Dong Z, Tai W, Lei W, et al., 2016, IL-27 Inhibits the TGF-β1-Induced Epithelial-Mesenchymal Transition in Alveolar Epithelial Cells. BMC Cell Biol, 17: 7.

[39] Chu L, Zhuo J, Huang H, et al., 2024, Tetrandrine Alleviates Pulmonary Fibrosis by Inhibiting Alveolar Epithelial Cell Senescence through PINK1/Parkin-Mediated Mitophagy. Eur J Pharmacol, 969: 176459.

[40] Liu T, Gonzalez De Los Santos F, Hirsch M, et al., 2021, Noncanonical Wnt Signaling Promotes Myofibroblast Differentiation in Pulmonary Fibrosis. Am J Respir Cell Mol Biol, 65(5): 489–499.

[41] Walker NM, Mazzoni SM, Vittal R, et al., 2018, c-Jun N-Terminal Kinase (JNK)-Mediated Induction of mSin1 Expression and mTORC2 Activation in Mesenchymal Cells During Fibrosis. J Biol Chem, 293(44): 17229–17239.

[42] Raghu G, Collard HR, Egan JJ, et al., 2011, An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-Based Guidelines for Diagnosis and Management. Am J Respir Crit Care Med, 183(6): 788–824.

[43] Petnak T, Lertjitbanjong P, Thongprayoon C, et al., 2021, Impact of Antifibrotic Therapy on Mortality and Acute Exacerbation in Idiopathic Pulmonary Fibrosis: A Systematic Review and Meta-Analysis. Chest, 160(5): 1751–1763.

[44] King TE Jr., Bradford WZ, Castro-Bernardini S, et al., 2014, A Phase 3 Trial of Pirfenidone in Patients with Idiopathic Pulmonary Fibrosis. N Engl J Med, 370(22): 2083–2092.

[45] Richeldi L, du Bois RM, Raghu G, et al., 2014, Nintedanib in Idiopathic Pulmonary Fibrosis. N Engl J Med, 370(22): 2071–2082.

[46] Kolb M, Egan JJ, Grossman J, et al., 2015, Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Management of Idiopathic Pulmonary Fibrosis. Am J Respir Crit Care Med, 192(2): e20–e40.

[47] Yusen RD, Edwards LB, Christie JD, et al., 2017, The Registry of the International Society for Heart and Lung Transplantation: 34th Official Adult Lung and Heart-Lung Transplant Report--2017; Focus Theme: Allograft Ischemic Time. J Heart Lung Transplant, 36(10): 1089–1103.